Title	Familiarity and Prudence of the Japanese Public with Research into Induced Pluripotent Stem Cells, and Their Desire for its Proper Regulation
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Familiarity and prudence of the Japanese public with research into induced pluripotent stem cells, and their desire for its proper regulation

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Abstract

The lack of knowledge of current public attitudes towards basic research into induced pluripotent stem cells (iPSCs) is a serious problem when considering appropriate ways of governance regarding research and its clinical applications. We therefore conducted an internet-based survey to determine public opinion regarding the research and development of iPSCs and regenerative medicine (RM). A total of 14,908 valid responses were collected, which revealed that the Japanese public were familiar with the terms iPSCs and RM, and many of them had received information about iPSCs and RM through the television and newspapers. They also generally accepted the need for extra funding for research into iPSCs, but also decided to adopt a “wait and see” approach and thought that research and development of

iPSCs and RM should be conducted under proper governance in accordance with an international regulatory framework. It will be necessary to discuss an internationally consistent regulatory system and effective mechanisms for information flow.

Key words: iPS cell, regenerative medicine, public attitude, internet-based survey, governance

Introduction

Science news from Japan and the United States in 2007 regarding the successful generation of induced pluripotent stem cells (iPSCs) through the direct reprogramming of somatic cells *in vitro* [1,2] traveled all over the world and impacted upon not only scientific fields, but also the public sphere. In Japan, iPSCs have been reported and discussed in all forms of media. Following a global trend to encourage the research and development of iPSCs and derived products in light of their expected impact, importance and benefits, the Japanese Ministry of Education, Sports, Culture, Science and Technology (MEXT) decided to invest 10 billion yen into promoting the research and development of iPSCs over a 5-year period beginning March 2008 [3].

The importance of adequate governance of advanced science has been discussed previously [4,5], and this applies to stem cell research. Many factors need to be considered in order to ensure proper governance, including social climate and public opinion. Several studies concerning public opinion about stem cell research have been conducted [6–8], but few large-scale investigations have focused on public attitudes towards iPSCs. One exception was a telephone-based survey conducted by a research group at Virginia Commonwealth University (VCU). They asked 1,000

Americans their opinions regarding stem cells, including iPSCs [8]. To the best of our knowledge, no subsequent large-scale investigations into public attitudes towards iPSCs have been conducted, despite the rapid movement forward on governance, funding decisions and iPSC research and development, and the rapid broadcasting of iPSC issues by the mass media. Considering that iPSCs have opened a new dialogue with respect to the basic research and clinical applications of pluripotent stem cells (PSCs), the lack of knowledge on current public attitudes towards iPSCs is a serious problem. We therefore conducted an internet-based survey in conjunction with the Asahi newspaper, one of the most prestigious newspapers in Japan with a circulation of approximately eight million [9]. This survey was open to the public and sought to determine their opinions regarding the research and development of iPSCs and regenerative medicine (RM).

Methods

Questionnaire

This was a web-based survey. A questionnaire was sent to members of the Asahi newspaper portal site and readers of the Asahi newspaper. Because public attitudes towards iPSCs and RM in Japan are unknown, we designed the questions to determine the public attitude towards and their recognition of iPSCs and RM. This research focused on the public recognition of iPSCs and RM and their opinions concerning the future prospects for and necessary regulation of these techniques, and their willingness to be actively involved. The questionnaire contained 16 questions, including three questions concerning the respondents' backgrounds and a question allowing free description of the respondents' images of iPSCs and advanced life science research (Table 1). The results of this aspect of the questionnaire are not

discussed here. We provided a brief introduction to the current situation of iPSCs and RM research, where we aimed to offer information on both the potential benefits and risks of iPSCs and RM, based on the opinions of scientists and the information broadcast in the media. All the questions required the respondents to choose one answer that best described their attitude. A total of 14,908 valid responses were collected in the 5-day period from the 5th to 9 September 2008. We are unable to present all the data here, but report on some of the significant results regarding the current public attitudes to iPSCs and RM in Japan.

To reduce confusion and prevent the questionnaire being too diffuse, we did not ask about people's recognition of research into stem cells or embryonic stem (ES) cells. Although many Japanese people seem to be aware of the terms ES cells and stem cells, it seemed likely that they would not know the difference between different types of stem cells. It was therefore decided that this research would focus on iPSCs and RM, which are the most significant and popular topics with the public in the field of advanced life sciences. A detailed investigation of public attitudes towards other types of stem cell research will follow.

Potential biases

The nature of internet-based research is associated with a potential for bias. While it has the advantages of low cost, rapid and easy collection of answers, easy limitation of target respondents, etc., possible disadvantages include a bias towards wealthy and more highly-educated respondents (particularly towards older people who can easily access the internet) [10]. In addition, the respondents were all readers of the Asahi newspaper and internet users, and were therefore possibly more conscious of social problems and had easier internet access than would have been the case had respondents been sampled at random. There were also possible

biases in terms of age and sex ratios (Table 2). Respondents under the age of 20 were in a minority, and our results may therefore not adequately reflect the opinions of younger members of the public towards iPSC and RM. However, considering the large number of respondents (14,908), it seems likely that the results of this survey reflect the general Japanese public opinion towards iPSCs and RM.

Results

Demographics of respondents

The demographics of the respondents with regard to age and sex are shown in Table 2. Of the total 14,908 respondents, 63.2% were male and 36.8% were female. Concerning their ages, 0.8% were < 19 years, 3.8% were 20–29 years, 12.8% were 30–39 years, 27.7% were 40–49 years, 27.6% were 50–59 years, 20.0% were 60–69 years and 7.4% were over 70 years.

Recognition of iPSCs and RM by the Japanese public

There was surprisingly high recognition by the public of the terms iPSCs and RM. The term iPSCs was recognized by 73.7% of the respondents, while 87.3% recognized the term RM. The results of a cross analysis of recognition between iPSCs and RM are shown in Table 3. This result indicates that the majority of Japanese readers of the Asahi newspaper were aware of these terms.

Public attitudes to iPSCs and RM in Japan

Concerning the necessity for research and development of iPSCs and RM, 44.6% of respondents thought it “very necessary” and 45.7% thought it “necessary” (Fig. 1). In addition, 57.6% believed it should be encouraged with more research funding, while 17.0% believed it should be continued with the same level of funding (Fig. 2). This suggests that many respondents accepted the necessity for continued research and into iPSCs and RM, and the possible need for extra funding. With respect to sex- and age-related responses, there was a tendency for older and male respondents to be more positive supporters of iPSC and RM research (data not shown). A similar tendency was identified when respondents were asked about the prospect of RM becoming a reality; a total of 65.4% said they believed it would be possible “within 10 years” (Fig. 3). Regarding progress and competition in research into iPSCs and RM, 34.9% of the respondents thought that Japan should establish a pioneering research system, and 51.4% of the respondents believed that research and development should progress with international cooperation (Fig. 4).

Concerning respondents’ willingness to cooperate with research and development of iPSCs and RM, 21.6% said they would like to cooperate by offering cells and/or blood, but 69.4% said they would like to wait and see the results of further research. Only 9.1% of respondents said they did not wish to cooperate (Fig. 5).

With respect to the collection of information regarding iPSCs and RM, most people said they gained their information from the TV or internet, or from newspapers (73.5%). Contrary to this, 12.4% answered that they would like to search for information using the internet, and 6.0% said they would like to be informed through books or by attending seminars (Fig. 6). 60.0% of respondents had no experiences of conversations about iPSCs or RM.

We also determined opinions about the regulatory framework governing research and development into iPSCs and RM for medical applications. 63.0 % of

respondents thought that Japan should have a regulatory framework based on international guidelines, while 23.0% thought that Japan should establish a proper regulatory system specifically for the Japanese situation (Fig. 7). The ethical issues surrounding the use of iPSCs to produce germ cells caused 30.3% of participants to respond that they believed the production of germ cells from iPSCs should be banned, while 58.4% thought it should be allowed to progress as long as it was carefully managed and monitored within a regulatory framework (Fig. 8).

Discussion

Public Familiarity with and Prudence Regarding iPSCs

The Japanese public generally accepted the necessity for extra funding and research into iPSCs and RM, and believed that RM would be realized in the near future (Figs. 1–3). This high level of recognition of a new type of stem cell was not found in a previous study in the United States [8]. Although the results of these two studies cannot be directly compared, the differences suggest a rapid change in social recognition. Although further studies are necessary, it seems likely that the rapid increase in mass-media broadcasting of iPSCs topics over the past 2 years may be responsible for this increased recognition [11].

It is worth noting that the Japanese public was not motivated to actively cooperate with the research and development of iPSCs and RM by offering their blood or cells at this stage (Fig. 5), but preferred to adopt a “wait and see” approach. Although it is difficult to judge the true meaning of the answers to this survey, the “wait and see” option favored by the public seems to suggest a prudent approach. Interestingly, this implies that a high level of recognition and acceptance of the necessity for research into iPSCs and RM does not directly impact the public’s

motivation to actively cooperate. In order to investigate this point further, more detailed research into sources of information is needed, given that many people received their information on iPSCs and RM through the media (Fig. 6), and the amount and nature of this information is likely to affect public opinions. A previous study pointed out the possible correlation between public opinion and mass-media broadcasts regarding the issue of genetically modified food in Japan [12]. This aspect will be the subject of future research.

With regard to the sources of information, it should be emphasized that over 70% of the public received most of their information concerning iPSCs and RM solely from the television and newspapers (Fig. 6). Thus the cooperation between researchers, regulatory agencies and journalists is a critical factor when considering the flow of information. Active and effective disclosure of the latest developments in iPSC and RM research, including the risks involved, should be considered, because a balanced information supply is the basis for appropriate governance by the natural and social scientists, policymakers, journalists, and the public. The current situation, with increased interactions between scientists and journalists, works in a positive direction [13].

Requirement for Governance

It is important to recognize that the Japanese public thought that research and development of iPSCs and RM should be conducted under proper governance, in accordance with an international regulatory framework (Fig. 7). In addition, approximately half of the respondents thought that it was important to progress with research and development with international cooperation (Fig. 4). Thus the establishment of proper governance at the international level needs to be discussed, and discussions relating to the regulatory framework for research and development

into PSCs, including iPSCs, are currently being conducted at the highest levels worldwide. For example, several international guidelines concerning general research and the clinical application of PSCs were presented by the International Society for Stem Cell Research (ISSCR) [14,15]. However, the ISSCR is an academic society and their proposed guidelines cannot be legally enforced in all countries. Moreover, the pace of regulatory developments differs between countries. In January of this year, the United States FDA approved safety evaluations regarding the clinical applications of ES cells [16]. International consensus guidelines are required to cover the safety aspects of such research and its medical applications.

In order to formulate such international guidelines, it is imperative to actively involve regulatory agencies to oversee safety testing, risk evaluation of tumorigenicity and clinical research procedures for cellular therapeutics. Current reports that have discussed the tumorigenicity risk of PSCs have emphasized the importance of appropriate preclinical studies and have pointed out the necessity for rapid discussions on evaluating safety standards and the effectiveness of PSCs in clinical applications [17,18]. Yamanaka, one of the key researchers into iPSCs and RM, pointed out the risk of cancer due to iPSC implantation in long-term mouse experiments. He emphasized the importance of long-term safety and tumorigenicity risk evaluations [19]. Concerning this problem, a detailed description of regulatory systems will be needed, considering the potential problems that can arise from imperfect articulation of regulatory guidelines concerning the clinical applications of RM and biologics derived from stem cells [20].

In addition to the safety aspects, ethical aspects are also important. In this study, subjects were asked about the issue of making germ cell from iPSCs. More than half of the respondents thought that research should progress within a carefully established regulatory framework (Fig. 8). In Japan, a MEXT sub-committee approved the production of germ cells from PSCs for basic research

in December 2008, though the fertilization of germ cells derived from PSCs is banned [21]. In the present study, we were unable to investigate in detail the public opinion on research concerned with making germ cells from iPSCs. In addition, this investigation was conducted over a different time period from that when the political decision on moderating research into making germ cells from iPSCs was made. Further research into the changes in public opinion and social, political, and scientific changes is needed.

Thus, in order to address the public requirement for the development of proper regulatory frameworks, it will be necessary to establish an international consensus on regulatory frameworks that has domestic legal authority to govern stem cell research and its application in each country. An internationally consistent regulatory system will promote future worldwide research and development into iPSCs and RM

Conclusion

The results of this study show that the Japanese public was familiar with the terms iPSCs and RM, and that they generally accepted the necessity of research into iPSCs. At the same time, they decided to adopt a “wait and see” approach, and thought that research and development into iPSCs and RM should be conducted under the proper regulations, in accordance with an international regulatory framework. This seems to demonstrate the prudence of the Japanese public. In order to address the public requirements, it will be necessary to discuss an international consensus on regulatory frameworks that have an impact on domestic stem cell research and its application in each country. It is also important to consider the methods of information flow concerning iPSCs and RM, and further research into this issue will be conducted.

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Question sentence

- Do you know about iPS cells?
- Do you know about RM?
- How would you like to find out about iPS cells or RM?
- How long do you think it will take to realize RM?
- Which idea regarding research and development into iPS cells and RM is closest to your opinion?
- What do you think about the cost of research into iPS cells and RM?
- What do you think about the regulatory framework regarding the medical applications of research and development into iPS cells and RM?
- Which of the following ideas about the use of iPS cells to make germ cells is closest to your opinion?
- Do you think that research into iPS cells and RM is necessary?
- Do you mean 'Is there anyone you know who would like to know more about RM?', or 'Is there anyone you know who would like to receive RM?'
- Do you have any opportunity to talk about iPS cells or RM in your daily life?
- Would you be prepared to be actively involved in iPS cell research?
- What is your attitude towards research into iPS cells or advanced life sciences?
- How old are you
- What is your occupation?
- What is your sex?

Table.1 List of questions

%(n)	Male	Female	Total
Under 19	0.5% (72)	0.3% (52)	0.8% (124)
20's	1.5% (219)	2.3% (344)	3.8% (563)
30's	5.9% (882)	6.8% (1021)	12.8% (1903)
40's	16.3% (2435)	11.1% (1694)	27.7% (4129)
50's	17.6% (2625)	10.0% (1488)	27.6% (4113)
60's	15.1% (2249)	4.9% (731)	20.0% (2980)
Over 70	6.3% (945)	1.0% (151)	7.4% (1096)
Total	63.2% (9427)	36.8% (5481)	100% (14908)

Table 2. Demographics of respondents.

% (n)		Do you know RM? Yes	No	Total
Do you know iPS cell?	Yes	72.1% (10743)	1.7% (246)	73.7% (10989)
	No	15.3% (2275)	11.0% (1644)	26.3% (3919)
	Total	87.3% (13018)	12.7% (1890)	100% (14908)

Table.3 Public familiarity with iPSCs and RM

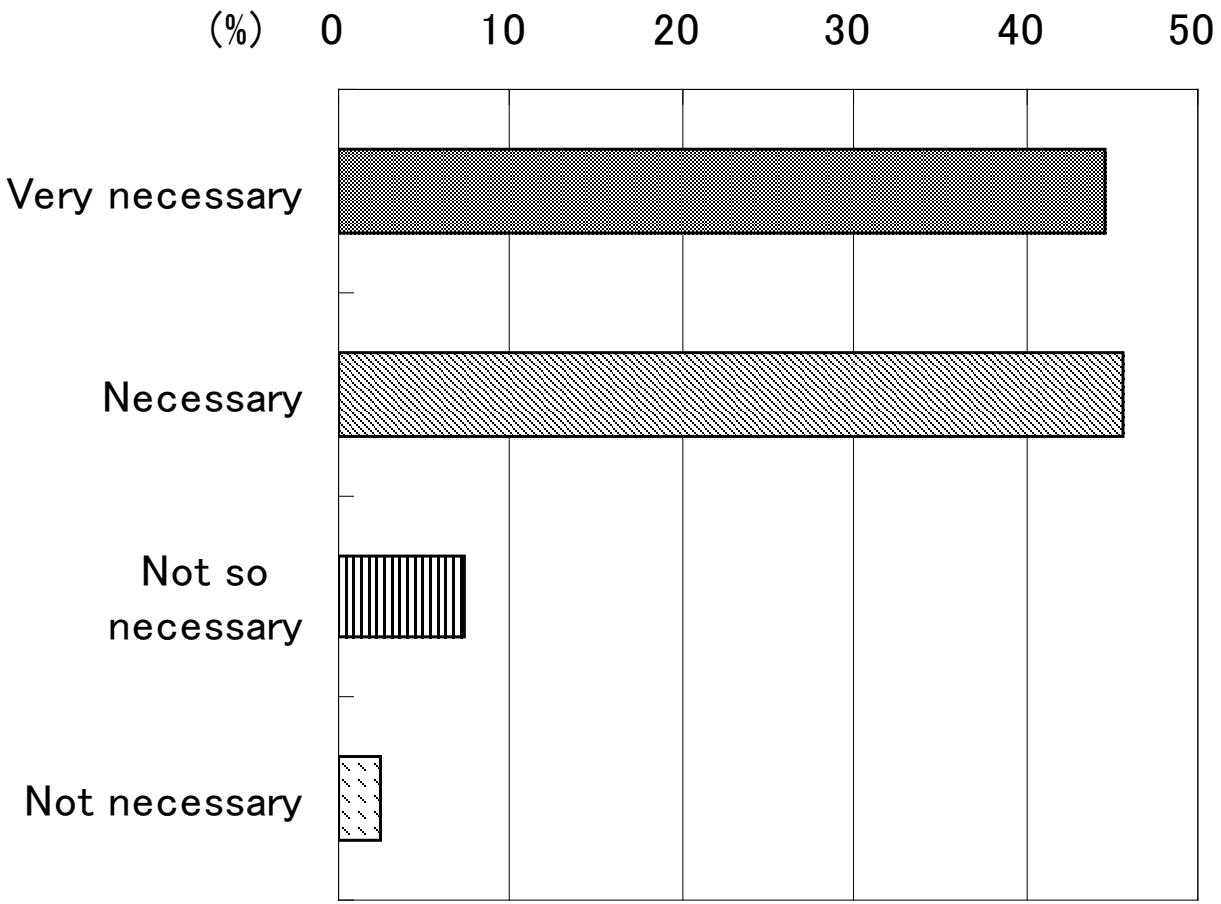

Figure.1 Do you think that research into iPS cells and RM is necessary?

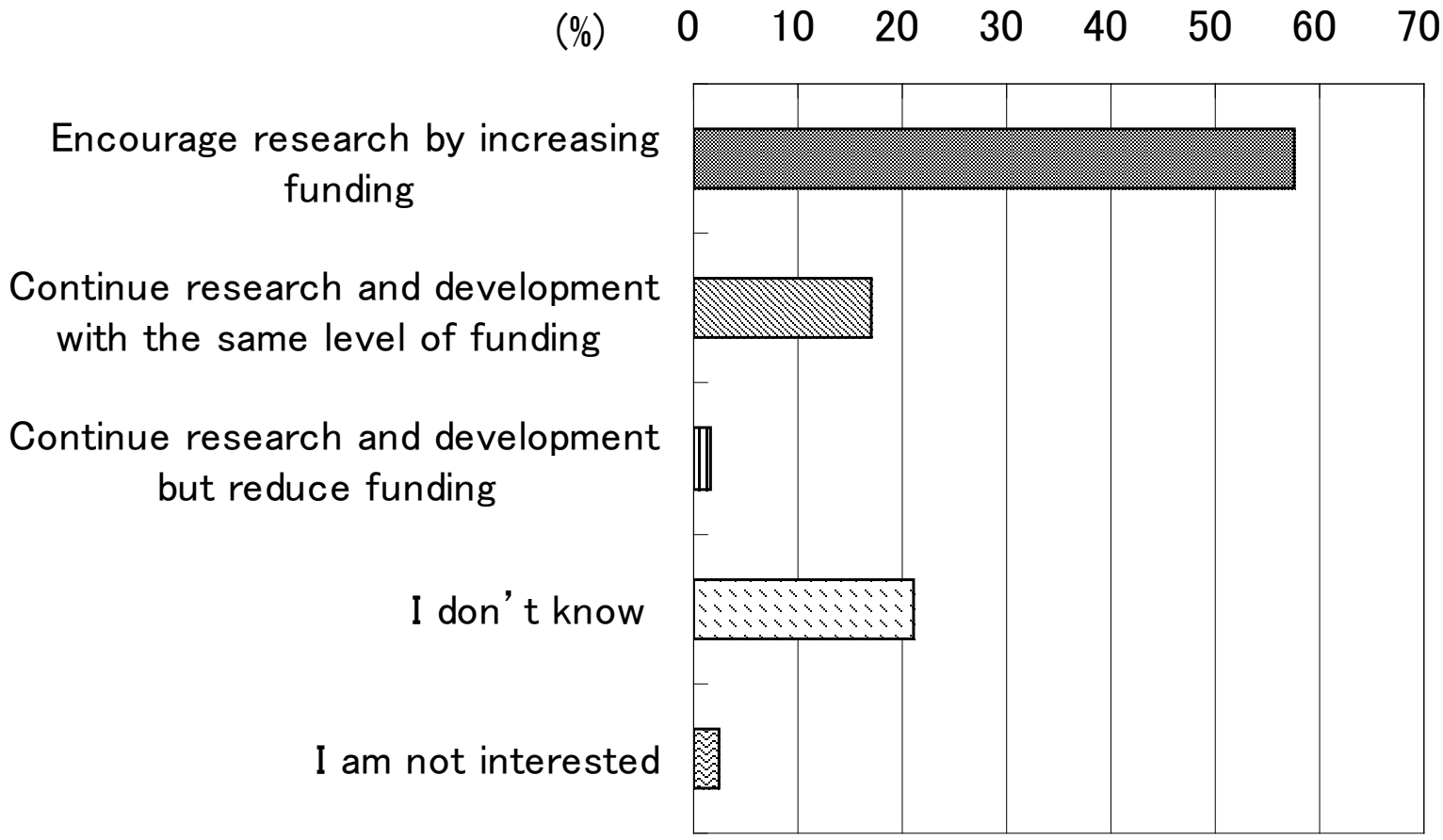

Figure.2 What do you think about the cost of research into iPS cells and RM?

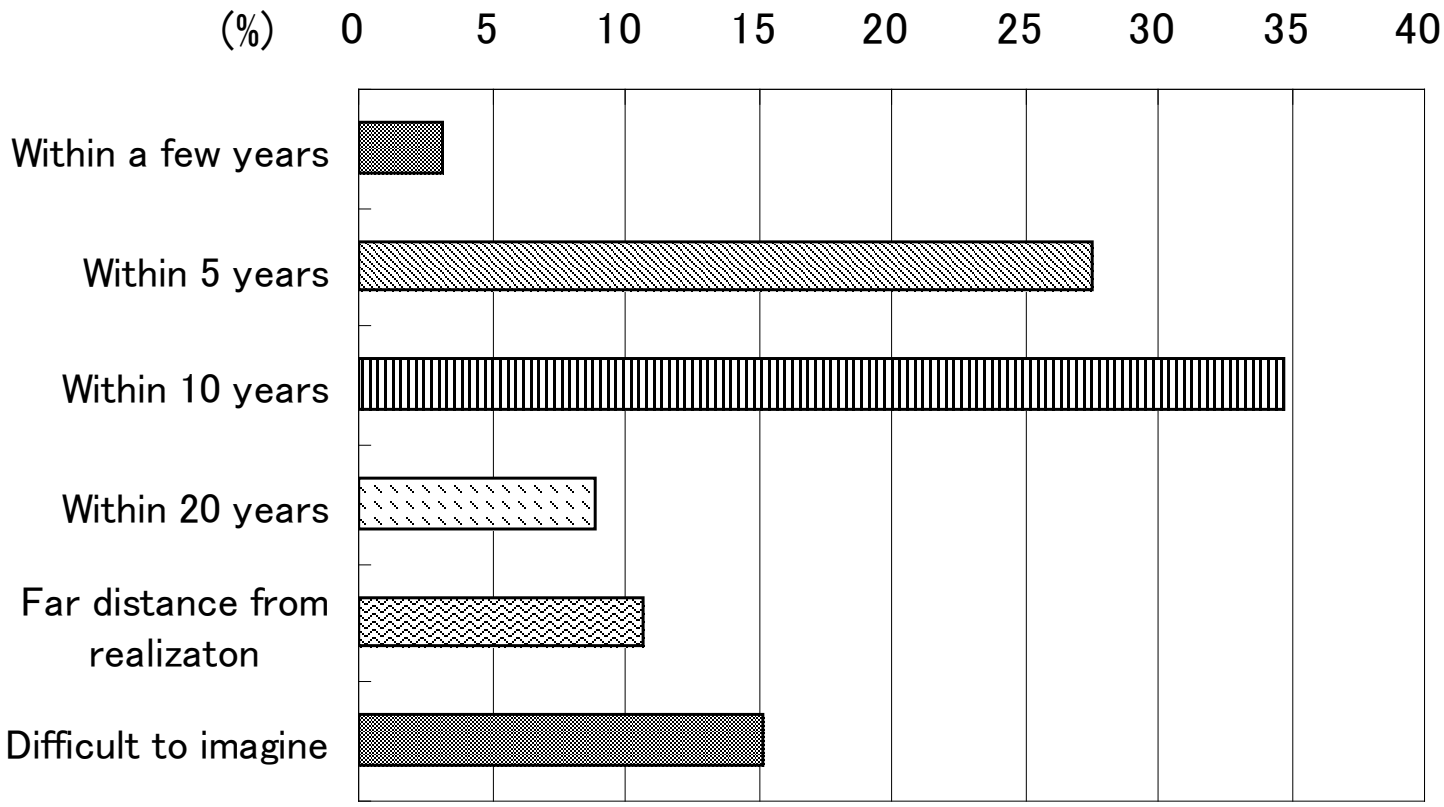

Figure.3 How long do you think it will take to realize RM?

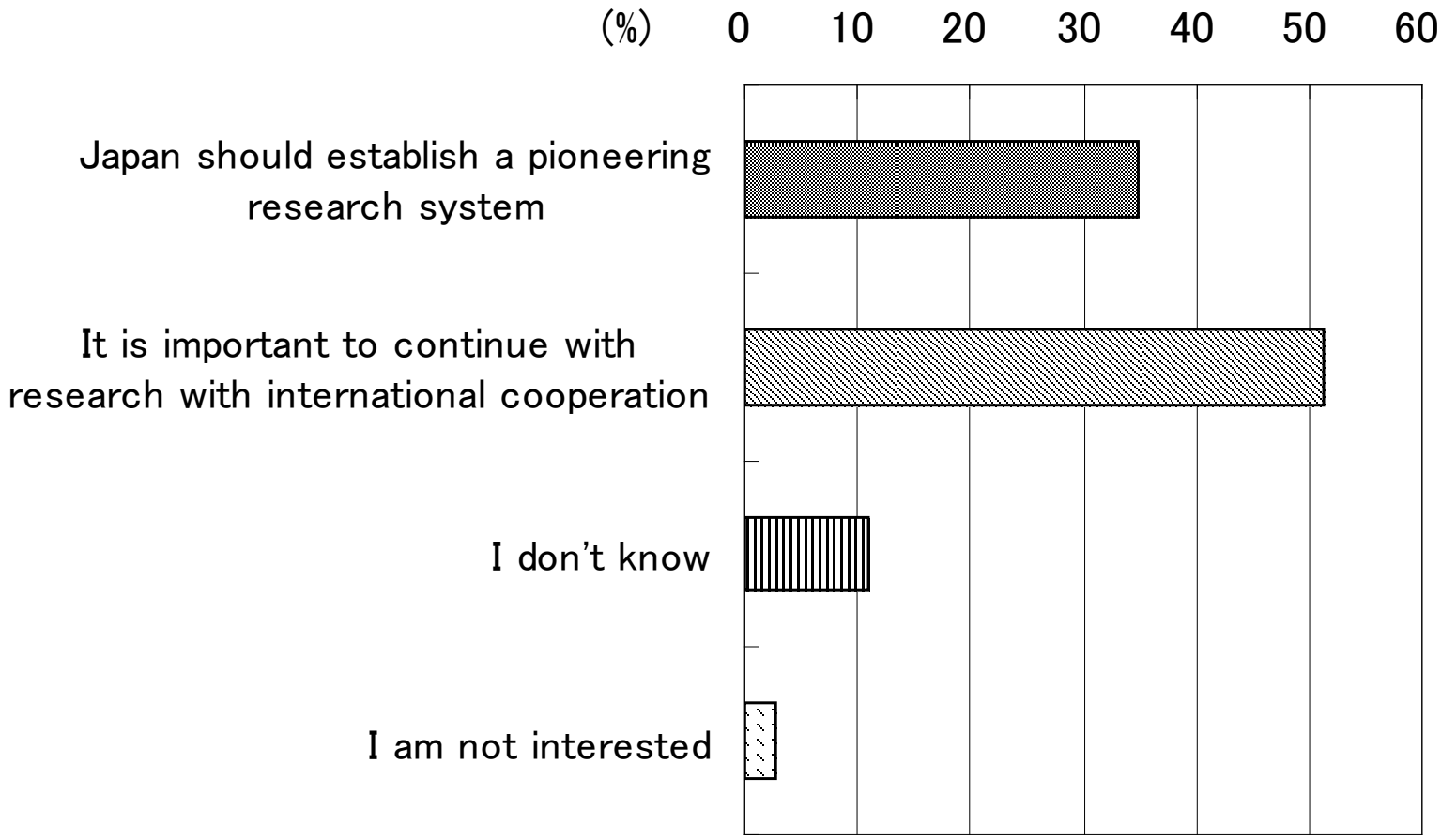

Figure.4 Which idea regarding research and development into iPS cells and RM is closest to your opinion?

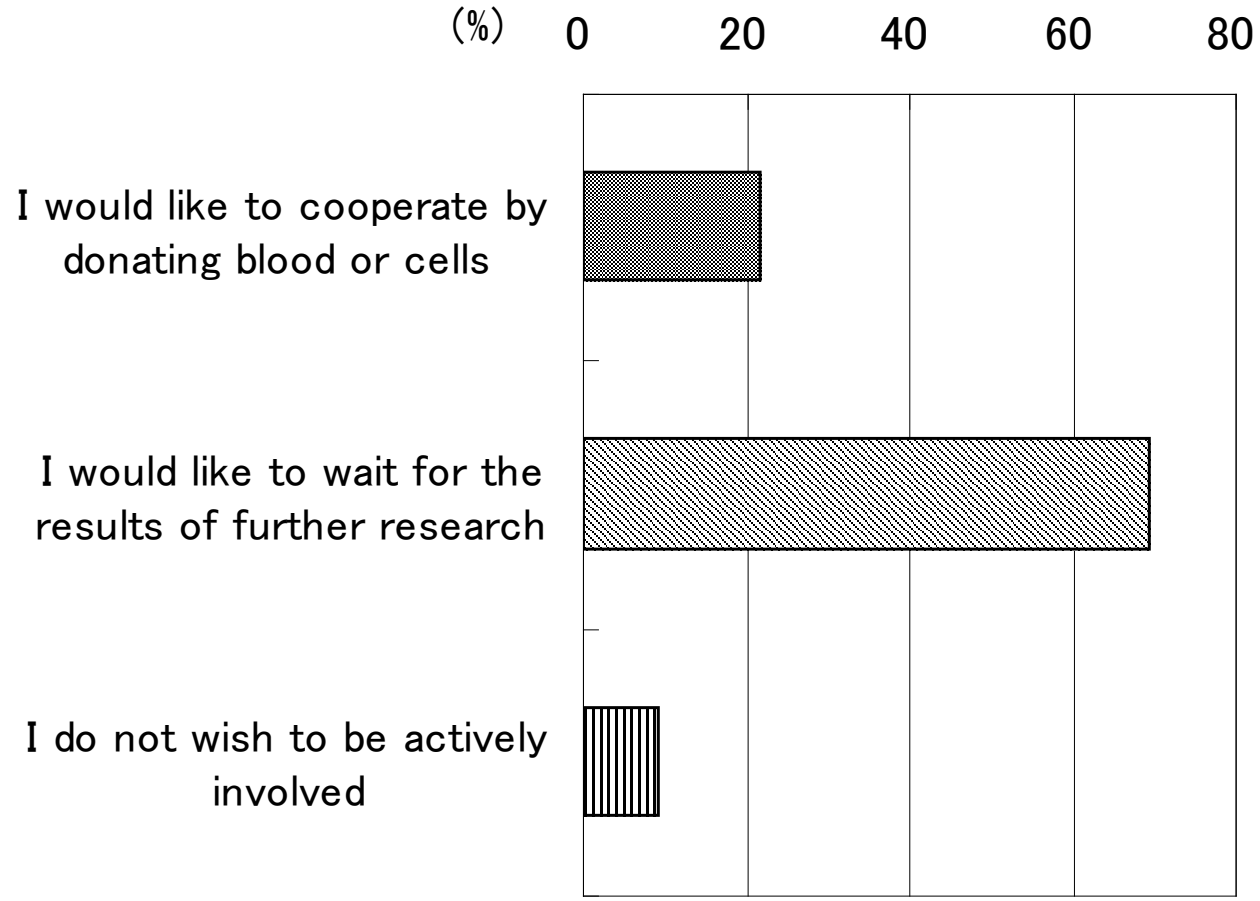

Figure.5 Would you be prepared to be actively involved in iPS cell research?

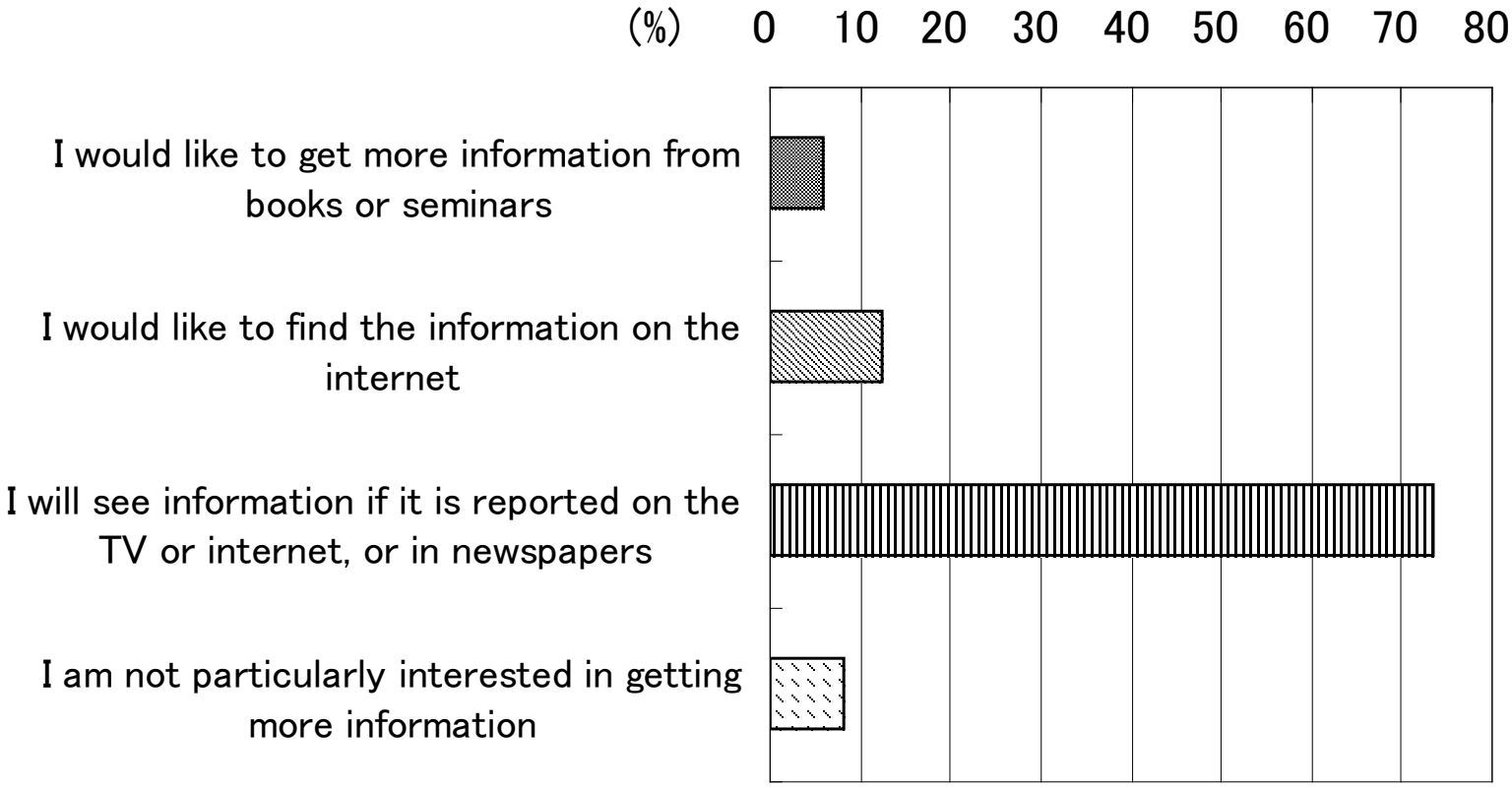

Figure.6 How would you like to find out about iPS cells or RM?

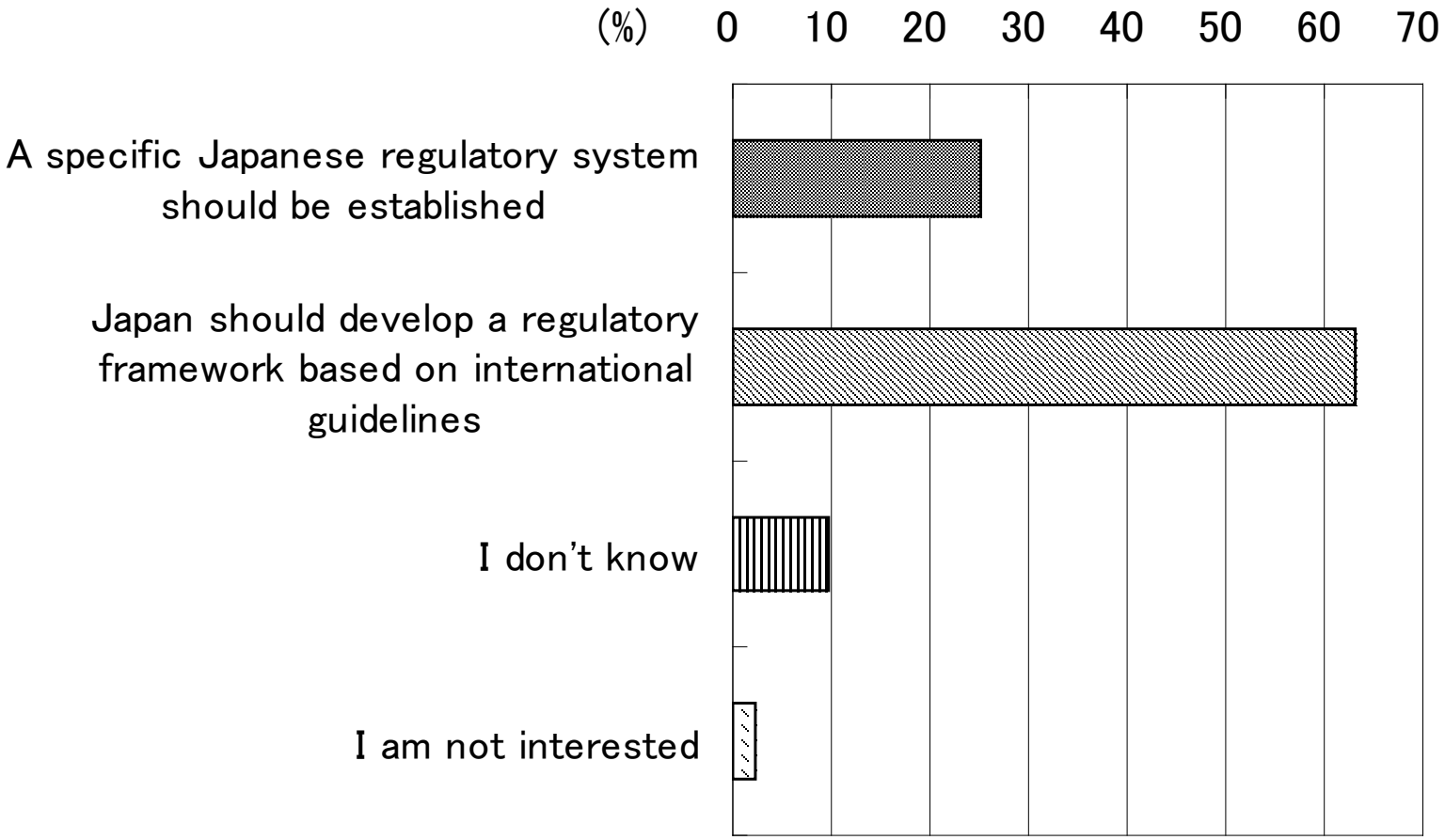

Figure.7 What do you think about the regulatory framework regarding the medical applications of research and development into iPS cells and RM?

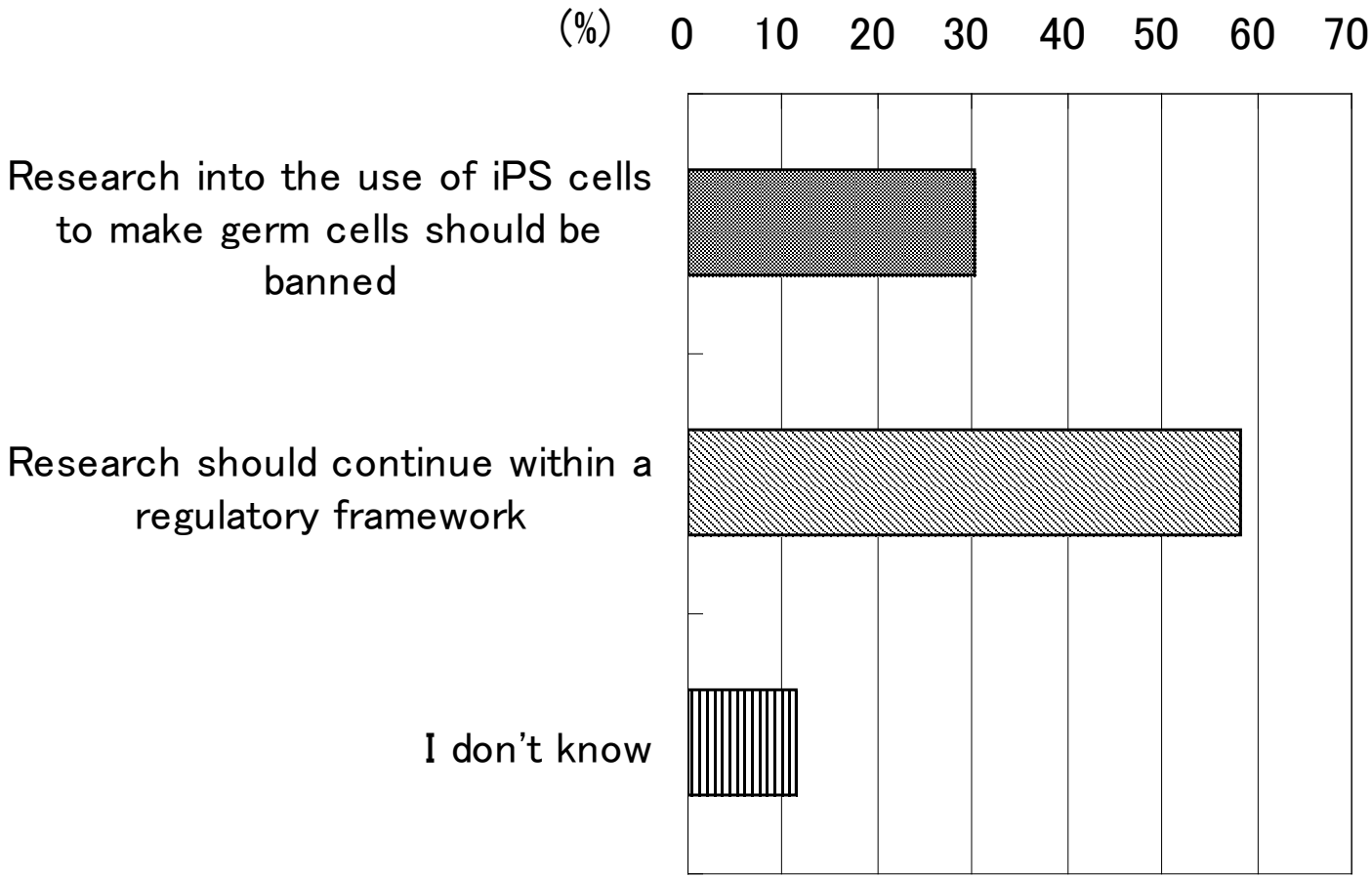

Figure.8 Which of the following ideas about the use of iPS cells to make germ cells is closest to your opinion?